

**AMENDMENT TO THE CLAIMS**

▪ **Format of Claim Amendments**

Applicant has amended the claims as indicated below. Pursuant to the revised format to 37 C.F.R. 1.121 adopted by the USPTO in July of 2003, Applicant herein submits only one version of the claims with markings to show changes. A detailed listing of all claims that are, or were in the application, are presented.

**COMPLETE LIST OF CLAIMS THAT ARE OR HAVE BEEN BEFORE THE  
OFFICE AFTER ENTRANCE OF THE AMENDMENTS MADE HEREIN (next Page)**

**1. (PREVIOUSLY PRESENTED)** A method of screening for inhibitors of beta-amyloid production comprising,

- 1) contacting a potential inhibitor of beta-amyloid production and a tagged inhibitor of beta-amyloid production with at least one macromolecule involved in the processing of APP and the production of beta-amyloid peptide, wherein the macromolecule is a secretase selected from alpha-secretase, beta-secretase, and gamma-secretase, said macromolecule containing a binding site specific for said tagged inhibitor of beta-amyloid production;
- 2) separating the tagged inhibitor of beta-amyloid production bound to said macromolecule from the tagged inhibitor of beta-amyloid production free from said macromolecule; and
- 3) determining an inhibitory concentration of the potential inhibitor of beta-amyloid production from the concentration of tagged inhibitor of beta-amyloid production bound to said macromolecule.

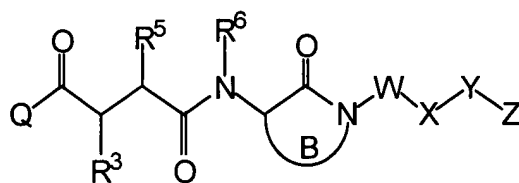
**2. (ORIGINAL)** The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production, a fluorescence labeled inhibitor of beta-amyloid production or a biotin labeled inhibitor of beta-amyloid production.

**3. (ORIGINAL)** The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production.

**4. (ORIGINAL)** The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a tritium or iodine radiolabeled inhibitor of beta-amyloid production.

**5. (ORIGINAL)** The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a tritium radiolabeled inhibitor of beta-amyloid production.

**6. (CURRENTLY AMENDED)** The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (I):



(I)

wherein:

at least one atom of the compound of the Formula (I) is radiolabeled;

Q is  $\text{NH}_2$ ;

R<sup>3</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-1 R<sup>4</sup>;

R<sup>4</sup> is H, OH, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> carbocycle, C<sub>6</sub>-C<sub>10</sub> aryl, or 5 to 10 membered heterocycle;

R<sup>5</sup> is H, OR<sup>14</sup>;

C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-3 R<sup>5b</sup>;

C<sub>1</sub>-C<sub>6</sub> alkoxy substituted with 0-3 R<sup>5b</sup>;

C<sub>2</sub>-C<sub>6</sub> alkenyl substituted with 0-3 R<sup>5b</sup>;

C<sub>2</sub>-C<sub>6</sub> alkynyl substituted with 0-3 R<sup>5b</sup>;

C<sub>3</sub>-C<sub>10</sub> carbocycle substituted with 0-3 R<sup>5c</sup>;

aryl substituted with 0-3 R<sup>5c</sup>; or

5 to 10 membered heterocycle substituted with 0-3 R<sup>5c</sup>;

**R<sup>5b</sup>**, at each occurrence, is independently selected from:

H, C<sub>1</sub>-C<sub>6</sub> alkyl, CF<sub>3</sub>, OR<sup>14</sup>, Cl, F, Br, I, =O, CN, NO<sub>2</sub>, NR<sup>15</sup>R<sup>16</sup>;

C<sub>3</sub>-C<sub>10</sub> carbocycle substituted with 0-3 R<sup>5c</sup>;

aryl substituted with 0-3 R<sup>5c</sup>; or

5 to 10 membered heterocycle substituted with 0-3 R<sup>5c</sup>;

R<sup>5c</sup>, at each occurrence, is independently selected from H, OH, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, Cl,

F, Br, I, CN, NO<sub>2</sub>, NR<sup>15</sup>R<sup>16</sup>, or CF<sub>3</sub>;

$R^6$  is H;

C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 0-3 R<sup>6a</sup>;

C<sub>3</sub>-C<sub>10</sub> carbocycle substituted with 0-3 R<sup>6b</sup>; or

aryl substituted with 0-3R<sup>6b</sup>;

R<sup>6a</sup>, at each occurrence, is independently selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, OR<sup>14</sup>, Cl, F, Br, I, =O,

CN, NO<sub>2</sub>, NR<sup>15</sup>R<sup>16</sup>, phenyl or CF<sub>3</sub>;

R<sup>6b</sup>, at each occurrence, is independently selected from H, OH, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, Cl,

F, Br, I, CN, NO<sub>2</sub>, NR<sup>15</sup>R<sup>16</sup>, or CF<sub>3</sub>;

W is -(CR<sup>8</sup>R<sup>8a</sup>)<sub>p</sub>-;

p is 0 to 4;

R<sup>8</sup> and R<sup>8a</sup>, at each occurrence, are independently selected from H, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl,

C<sub>2</sub>-C<sub>4</sub> alkynyl and C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

X is a bond;

C<sub>6</sub>-C<sub>10</sub> aryl substituted with 0-3 R<sup>Xb</sup>;

C<sub>3</sub>-C<sub>10</sub> carbocycle substituted with 0-3 R<sup>Xb</sup>; or

5 to 10 membered heterocycle substituted with 0-3 R<sup>Xb</sup>;

R<sup>Xb</sup>, at each occurrence, is independently selected from H, OH, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, Cl,

F, Br, I, CN, NO<sub>2</sub>, NR<sup>15</sup>R<sup>16</sup>, or CF<sub>3</sub>;

Y is a bond or -(CR<sup>9</sup>R<sup>9a</sup>)<sub>t</sub>-V-(CR<sup>9</sup>R<sup>9a</sup>)<sub>u</sub>-;

t is 0 to 3;

u is 0 to 3;

R<sup>9</sup> and R<sup>9a</sup>, at each occurrence, are independently selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>3</sub>-C<sub>8</sub>

cycloalkyl;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -N(R<sup>19</sup>)-, -C(=O)NR<sup>19b</sup>-, -NR<sup>19b</sup>C(=O)-, -

NR<sup>19b</sup>S(=O)<sub>2</sub>-, -S(=O)<sub>2</sub>NR<sup>19b</sup>-, -NR<sup>19b</sup>S(=O)-, -S(=O)NR<sup>19b</sup>-, -C(=O)O-, or -OC(=O)-;

Z is H;

C<sub>1</sub>-C<sub>8</sub> alkyl substituted with 0-2 R<sup>12</sup>;

C<sub>2</sub>-C<sub>4</sub> alkenyl substituted with 0-2 R<sup>12</sup>;

C<sub>2</sub>-C<sub>4</sub> alkynyl substituted with 0-2 R<sup>12</sup>;

aryl substituted with 0-4 R<sup>12b</sup>;

C<sub>3</sub>-C<sub>10</sub> carbocycle substituted with 0-4 R<sup>12b</sup>; or

5 to 10 membered heterocycle substituted with 0-3 R<sup>12b</sup>;

R<sup>12</sup> is aryl substituted with 0-4 R<sup>12b</sup>;

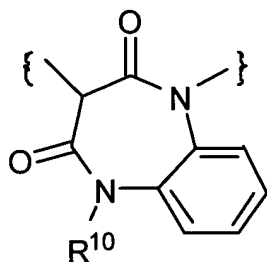
C<sub>3</sub>-C<sub>10</sub> carbocycle substituted with 0-4 R<sup>12b</sup>; or

5 to 10 membered heterocycle substituted with 0-3 R<sup>12b</sup>;

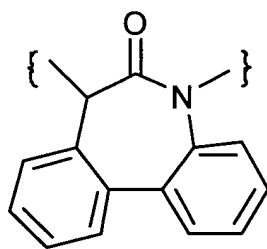
R<sup>12b</sup>, at each occurrence, is independently selected from H, OH, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, Cl,

F, Br, I, CN, NO<sub>2</sub>, NR<sup>15</sup>R<sup>16</sup>, or CF<sub>3</sub>;

B is



or



R<sup>10</sup> is H, C(=O)R<sup>17</sup>, C(=O)OR<sup>17</sup>, C(=O)NR<sup>18</sup>R<sup>19</sup>,

S(=O)<sub>2</sub>NR<sup>18</sup>R<sup>19</sup>, S(=O)<sub>2</sub>R<sup>17</sup>;

C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with R<sup>10a</sup>;

aryl substituted with 0-4 R<sup>10b</sup>;

C<sub>3</sub>-C<sub>10</sub> carbocycle substituted with 0-3 R<sup>10b</sup>; or

5 to 10 membered heterocycle optionally substituted with 0-3 R<sup>10b</sup>;

R<sup>10a</sup>, at each occurrence, is independently selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl,

OR<sup>14</sup>, Cl, F, Br, I, =O, CN, NO<sub>2</sub>, NR<sup>15</sup>R<sup>16</sup>, phenyl or CF<sub>3</sub>;

R<sup>10b</sup>, at each occurrence, is independently selected from H, OH, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, Cl,

F, Br, I, CN, NO<sub>2</sub>, NR<sup>15</sup>R<sup>16</sup>, or CF<sub>3</sub>;

R<sup>14</sup> is H, phenyl, benzyl, C<sub>1</sub>-C<sub>6</sub> alkyl, or C<sub>2</sub>-C<sub>6</sub> alkoxyalkyl;

R<sup>15</sup>, at each occurrence, is independently selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, benzyl, phenethyl, -

C(=O)-(C<sub>1</sub>-C<sub>6</sub> alkyl) and -S(=O)<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl);

R<sup>16</sup>, at each occurrence, is independently selected from H, OH, C<sub>1</sub>-C<sub>6</sub> alkyl, benzyl, phenethyl, -

C(=O)-(C<sub>1</sub>-C<sub>6</sub> alkyl) and -S(=O)<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl);

R<sup>17</sup> is H, phenyl, benzyl, C<sub>1</sub>-C<sub>6</sub> alkyl, or C<sub>2</sub>-C<sub>6</sub> alkoxyalkyl;

R<sup>18</sup>, at each occurrence, is independently selected from H, C<sub>1</sub>-C<sub>6</sub> alkyl, benzyl, phenethyl, -

C(=O)-(C<sub>1</sub>-C<sub>6</sub> alkyl) and -S(=O)<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl); and

R<sup>19</sup>, at each occurrence, is independently selected from H, OH, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, benzyl,

phenethyl, -C(=O)-(C<sub>1</sub>-C<sub>6</sub> alkyl) and -S(=O)<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl); and

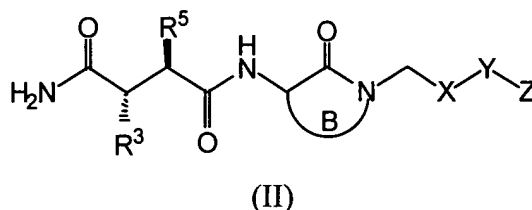
R<sup>19b</sup> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, benzyl or phenethyl; ~~and~~

~~R<sup>20</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl.~~

7. (ORIGINAL) The method of Claim 6 wherein R<sup>3</sup> is C<sub>3</sub>-C<sub>6</sub> alkyl.

8. (ORIGINAL) The method of Claim 6 wherein R<sup>3</sup> is C<sub>3</sub>-C<sub>6</sub> alkyl substituted with about 1 to about 4 <sup>3</sup>H.

9. (ORIGINAL) The method of Claim 6 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (II):



wherein:

at least one atom of the compound of the Formula (II) is radiolabeled.

**10. (ORIGINAL)** The method of Claim 9 wherein R<sup>3</sup> is C<sub>3</sub>-C<sub>6</sub> alkyl substituted with about 1 to about 4 <sup>3</sup>H.

**11. - 12 (CANCELLED)**

**13. (PREVIOUSLY PRESENTED)** The method of Claim 1 wherein at least one macromolecule involved in the processing of APP and the production of beta-amyloid peptide comprises alpha-, beta- or gamma-secretase

**14. (CURRENTLY AMENDED)** The method of Claim 1 wherein at least one macromolecule involved in the processing of APP and/or the production of beta-amyloid peptide comprises:

- (1)  $\beta$  secretase;
- (2)  $\alpha$  secretase; or
- (3)  $\gamma$  secretase;

or any fragment or derivative thereof; said macromolecule containing a binding site specific for said tagged inhibitor of beta-amyloid production.

**15. (ORIGINAL)** The method of Claim 1 wherein the inhibitory concentration is half maximal inhibitory concentration.

**16. (CURRENTLY AMENDED)** A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of an inhibitor of beta-amyloid production identified by the screening assay of Claim 1 or a pharmaceutically acceptable salt or prodrug form thereof.

**17. (CURRENTLY AMENDED)** A method for treating degenerative neurological disorders involving similar to Alzheimer's Disease, accumulative beta-amyloid production comprising administering to a host in need of such treatment a therapeutically effective amount of an inhibitor of beta-amyloid production identified by the screening assay of Claim 1 or a pharmaceutically acceptable salt form thereof.

**18. (PREVIOUSLY PRESENTED)** A method for treating Alzheimer's disease comprising administering to a host in need of such treatment a therapeutically effective amount of an inhibitor of beta-amyloid production identified by the screening assay of Claim 1 or a pharmaceutically acceptable salt form thereof.

**19. (CANCELLED)**

**20. (PREVIOUSLY PRESENTED)** The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production, a fluorescence labeled inhibitor of beta-amyloid production, or a biotin labeled inhibitor of beta-amyloid production.

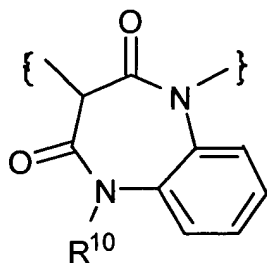
**21. (PREVIOUSLY PRESENTED)** The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production.

**22. (CURRENTLY AMENDED)** The method of Claim 1 wherein the tagged inhibitor is radiolabeled with one or more radioisotope selected from  $^3\text{H}$ ,  $^{11}\text{C}$ ,  $^{14}\text{C}$ ,  $^{18}\text{F}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ , and  $^{131}\text{I}$ .

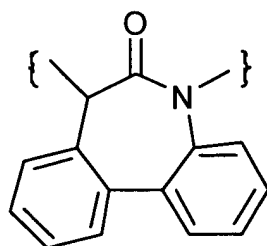
**23.-35. (CANCELLED)**

**36. (PREVIOUSLY PRESENTED)** An inhibitor of beta-amyloid production comprising a compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula as claimed in claim 1 wherein ring B is





or



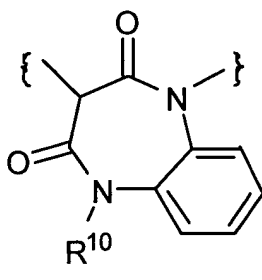
**37. (CURRENTLY AMENDED)** An inhibitor of beta-amyloid production of Claim 36 wherein the macromolecule involved in the production of beta-amyloid peptide is alpha-secretase, beta-secretase, or gamma-secretase, or a fragment thereof, containing a binding site specific for said tagged inhibitor of beta-amyloid production.

**38. (CURRENTLY AMENDED)** An inhibitor of beta-amyloid production of Claim 36 wherein the macromolecule involved in the production of beta-amyloid peptide is gamma-secretase or a fragment thereof, containing a binding site specific for said tagged inhibitor of beta-amyloid production.

**39. (CURRENTLY AMENDED)** An inhibitor of beta-amyloid production of Claim 36 comprising a compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said compound demonstrates a half maximal inhibitory concentration of less than 10 micromolar for beta-amyloid production.

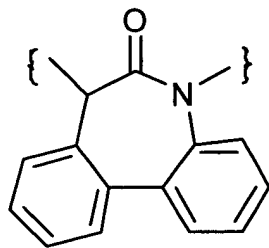
**40. (CURRENTLY AMENDED)** An inhibitor of beta-amyloid production of Claim 36 comprising a compound which interacts with a binding site on gamma-secretase or a fragment of gamma-secretase; wherein the compound demonstrates a half maximal inhibitory concentration of less than 10 micromolar for beta-amyloid production.

**41. (CURRENTLY AMENDED)** An inhibitor of beta-amyloid production of Claim 6 comprising a compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula (I) wherein B is



and the compound demonstrates a half maximal inhibitory concentration of less than 10 micromolar for beta-amyloid production.

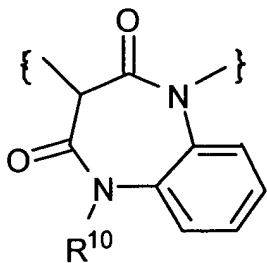
**42. (CURRENTLY AMENDED)** An inhibitor of beta-amyloid production of Claim 6 comprising a compound which interacts with a binding site on gamma-secretase or a fragment of gamma-secretase; wherein said binding site is a specific binding site for a compound of Formula (I) wherein B is



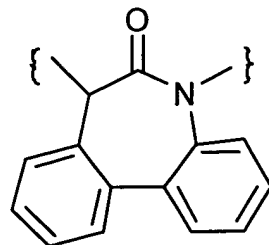
;B

and the compound demonstrates a half maximal inhibitory concentration of less than 10 micromolar for beta-amyloid production.

**43. (PREVIOUSLY PRESENTED)** A tagged inhibitor of beta-amyloid production of Claim 6 comprising a tagged compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula (I) wherein ring B is:



or



**44. (CURRENTLY AMENDED)** A tagged inhibitor of beta-amyloid production of Claim 43 wherein the macromolecule involved in the production of beta-amyloid peptide is alpha-, beta-,

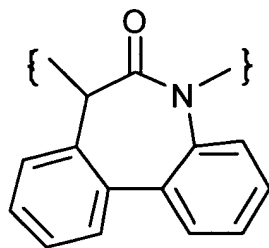
or gamma-secretase or a fragment thereof, containing a binding site specific for said tagged inhibitor of beta-amyloid production.

**45. (CURRENTLY AMENDED)** A tagged inhibitor of beta-amyloid production of Claim 43 wherein the macromolecule involved in the production of beta-amyloid peptide is gamma-secretase or a fragment thereof, containing a binding site specific for said tagged inhibitor of beta-amyloid production.

**46. (CURRENTLY AMENDED)** A tagged inhibitor of beta-amyloid production of Claim 43 comprising a tagged compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said tagged compound demonstrates a half maximal inhibitory concentration of less than 10 micromolar for beta-amyloid production.

**47. (CURRENTLY AMENDED)** A tagged inhibitor of beta-amyloid production of Claim 43 comprising a tagged compound which interacts with a binding site on alpha-, beta-, or gamma-secretase or a fragment thereof; wherein said tagged compound demonstrates a half maximal inhibitory concentration of less than 10 micromolar for beta-amyloid production.

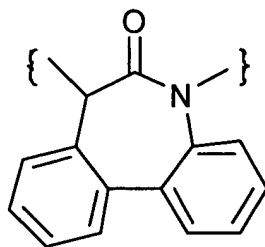
**48. (CURRENTLY AMENDED)** A tagged inhibitor of beta-amyloid production of Claim 6 comprising a tagged compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula (I) wherein ring B is



;

and the tagged compound demonstrates a half maximal inhibitory concentration of less than 10 micromolar for beta-amyloid production.

**49. (CURRENTLY AMENDED)** A tagged inhibitor of beta-amyloid production of Claim 48 comprising a tagged compound which interacts with a binding site on presenilin 1 or a fragment of presenilin 1; wherein said binding site is a specific binding site for a compound of Formula (I) wherein ring B is:



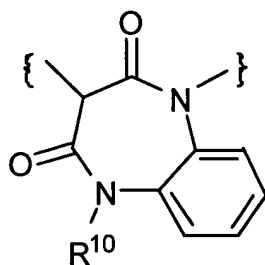
;

and the tagged compound demonstrates a half maximal inhibitory concentration of less than 10 micromolar for beta-amyloid production.

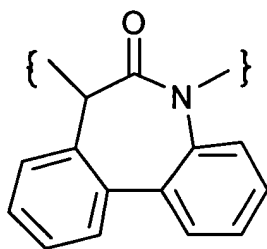
**50. – 53. (CANCELLED)**

**54. (PREVIOUSLY PRESENTED)** A method of treating Alzheimer's disease comprising administering to a host in need of such treatment a therapeutically effective amount of an inhibitor of beta-amyloid production, or a pharmaceutically acceptable salt form thereof, wherein said inhibitor of beta-amyloid production binds to a binding site on a macromolecule involved in the production of beta-amyloid peptide and effects a decrease in production of beta-amyloid peptide;

wherein said binding site is a specific binding site for a compound of Formula (I) of Claim 6 wherein ring B is:

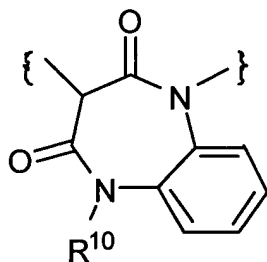


or



**55. (CURRENTLY AMENDED)** The method of Claim 54 wherein the macromolecule comprises ~~alpha~~  $\alpha$  - secretase, ~~beta~~  $\beta$  - secretase, or ~~gamma~~  $\gamma$  -secretase, or a fragment thereof, containing a binding site specific for said tagged inhibitor of beta-amyloid production.

**56. (PREVIOUSLY PRESENTED)** A method of Claim 54 wherein the binding site is a specific binding site for a compound of Formula (I) wherein ring B is:



**57. (CURRENTLY AMENDED)** The method of Claim 56 wherein the macromolecule comprises ~~alpha~~  $\alpha$  secretase, ~~beta~~  $\beta$  secretase, or ~~gamma~~  $\gamma$  secretase, or a fragment thereof, containing a binding site specific for said tagged inhibitor of beta-amyloid production.

**58. (CURRENTLY AMENDED)** The method of Claim 56 wherein the macromolecule comprises  $\gamma$  ~~gamma~~-secretase, or a fragment thereof, containing a binding site specific for said tagged inhibitor of beta-amyloid production.

**59. (PREVIOUSLY PRESENTED)** A method of *in vivo* diagnostic imaging comprising administering to a subject a diagnostically effective amount of a radiolabeled inhibitor of Claim 6 of beta-amyloid production.

**60. (ORIGINAL)** A method of Claim 59 wherein said method is used in the diagnosis of a neurological disease which involves APP processing or elevated levels of beta-amyloid, or both.

**61. (ORIGINAL)** A method of Claim 59 wherein said method is used in the diagnosis of Alzheimer's disease.

**62. (ORIGINAL)** A method of Claim 59 wherein the radiolabeled inhibitor is suitable for imaging of the brain of the subject.

**63. (CURRENTLY AMENDED)** A method of Claim 59 wherein the radiolabeled inhibitor is radiolabeled with one or more radioisotope selected from  $^3\text{H}$ ,  $^{11}\text{C}$ ,  $^{14}\text{C}$ ,  $^{18}\text{F}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ , and ~~or~~  $^{131}\text{I}$ .

**64. (CURRENTLY AMENDED)** A method of Claim 59 wherein the tagged inhibitor of beta-amyloid production is a compound selected from any compound found capable of binding a gamma-secretase or fragment thereof containing a binding site specific for said tagged inhibitor of beta-amyloid production, such as 5-amino-6-cyclohexyl-4-hydroxy-hexanamide derivatives, N-aryl amino acid esters, N-heteroaryl amino acid esters, N-arylacetyl amino acid amides, N-heteroarylacetyl amino acid amides, and N-alkylacetyl amino acid amides, N-arylacetyl amino acid esters, N-heteroarylacetyl amino acid esters, and N-alkylacetyl amino acid esters, N-aryl amino acid derivatives, N-heteroaryl amino acid derivatives, and cycloalkyl, lactam, lactone and related compounds

~~disclosed in or within the scope of compounds disclosed in a reference selected from:~~

- ~~(1) United States patent US 5,703,129;~~
- ~~(2) PCT application WO98/22441 (or its priority USSN 08/755,444);~~
- ~~(3) PCT application WO98/22433 (or its priority USSN 08/807,538);~~
- ~~(4) PCT application WO98/22430 (or its priority USSN 08/754,895);~~
- ~~(5) PCT application WO98/22493 (or its priority USSN 08/755,334);~~
- ~~(6) PCT application WO98/22494 (or its priorities USSN 08/808,528, 08/807,528 or 08/807,427);~~
- ~~(7) PCT application WO98/28268 (or its priority USSN 08/780,025);~~
- ~~(8) PCT application WO98/38177;~~
- ~~(9) PCT application WO95/09838~~
- ~~(10) PCT application WO99/67221;~~
- ~~(11) PCT application WO99/67220;~~
- ~~(12) PCT application WO99/67219;~~
- ~~(13) PCT application WO95/66934;~~
- ~~(14) PCT application WO00/24392; or~~
- ~~(15) Ghosh et al., JACS (2000) 122:3522-2523;~~

~~or any compound which inhibits beta-amyloid production and binds competitively with any of the foregoing compounds in any of the assays described in the Utility section hereof;~~  
~~all of which foregoing references are hereby incorporated by reference in their entirety.~~

**65. (CURRENTLY AMENDED)** A method of Claim 59 wherein the inhibitor of beta-  $\beta$  amyloid production exhibits activity as an inhibitor of ~~gamma-~~  $\gamma$  secretase.



**66. - 69. (CANCELLED)**

**70. (PREVIOUSLY PRESENTED)** A method of Claim 59 wherein the inhibitor of beta-amyloid production is selected from:

- (1) an inhibitor of  $\beta$  secretase;
- (2) an inhibitor of  $\alpha$  secretase; or
- (3) an inhibitor of  $\gamma$  secretase.

**71. (PREVIOUSLY PRESENTED)** A pharmaceutical composition comprising a compound of Claim 6 suitable for in vivo diagnostic imaging comprising a radiolabeled inhibitor of beta-amyloid production.

**72. (ORIGINAL)** A pharmaceutical composition of Claim 71 wherein the composition is used in the diagnosis of a neurological disease which involves APP processing or elevated levels of beta-amyloid, or both.

**73. (ORIGINAL)** A pharmaceutical composition of Claim 71 wherein the composition is used in the diagnosis of Alzheimer's disease.

**74. (ORIGINAL)** A pharmaceutical composition of Claim 71 wherein the radiolabeled inhibitor is suitable for imaging of the brain of the subject.

**75. (CURRENTLY AMENDED)** A pharmaceutical composition of Claim 71 wherein the radiolabeled inhibitor is radiolabeled with one or more radioisotope selected from  $^3\text{H}$ ,  $^{11}\text{C}$ ,  $^{14}\text{C}$ ,  $^{18}\text{F}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ , and ~~or~~  $^{131}\text{I}$ .

**76. (CURRENTLY AMENDED)** A pharmaceutical composition of Claim 71 wherein the inhibitor of beta-amyloid production is a compound selected from any compound found capable of binding a  $\beta$  secretase, or fragment thereof containing a binding site specific for said tagged inhibitor of beta-amyloid production,

such as 5-amino-6-cyclohexyl-4-hydroxy-hexanamide derivatives, N-aryl amino acid esters, N-heteroaryl amino acid esters, N-arylacetyl amino acid amides, N-heteroarylacetyl amino acid amides, and N-alkylacetyl amino acid amides, N-arylacetyl amino acid esters, N-heteroarylacetyl amino acid esters, and N-alkylacetyl amino acid esters, N-aryl amino acid derivatives, N-heteroaryl amino acid derivatives, and cycloalkyl, lactam, lactone and related compounds

~~disclosed in or within the scope of compounds disclosed in a reference selected from:~~

- ~~(1) United States patent US 5,703,129;~~
- ~~(2) PCT application WO98/22441 (or its priority USSN 08/755,444);~~
- ~~(3) PCT application WO98/22433 (or its priority USSN 08/807,538);~~
- ~~(4) PCT application WO98/22430 (or its priority USSN 08/754,895);~~
- ~~(5) PCT application WO98/22493 (or its priority USSN 08/755,334);~~
- ~~(6) PCT application WO98/22494 (or its priorities USSN 08/808,528, 08/807,528 or 08/807,427);~~
- ~~(7) PCT application WO98/28268 (or its priority USSN 08/780,025);~~
- ~~(8) PCT application WO98/38177;~~
- ~~(9) PCT application WO95/09838;~~
- ~~(10) PCT application WO99/67221;~~
- ~~(11) PCT application WO99/67220;~~
- ~~(12) PCT application WO99/67219;~~
- ~~(13) PCT application WO95/66934;~~
- ~~(14) PCT application WO00/24392; or~~
- ~~(15) Ghosh et al., JACS (2000) 122:3522-2523;~~

~~or any compound which inhibits beta-amyloid production and binds competitively with any of the foregoing compounds in any of the assays described in the Utility section hereof, all of which foregoing references are hereby incorporated by reference in their entirety.~~

**77. (PREVIOUSLY PRESENTED)** A pharmaceutical composition of Claim 71 wherein the inhibitor of beta-amyloid production is an inhibitor of  $\gamma$ -secretase.